Mass General Brigham
Health Plan

Enzyme and Metabolic Disorder Therapies
Effective 06/05/2023

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☒ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☒ Medical Benefit (NLX)		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Specialty Medications**		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	See Overview table below for drugs available through medical benefit only		

Overview

No PA	Require PA
Ammonul® # (sodium phenylacetate/sodium benzoate) Buphenyl® # (sodium phenylbutyrate powder, tablet) Creon® DR (pancrelipase) Pancreaze® DR (pancrelipase) † Pertzye® DR (pancrelipase) Viokace® (pancrelipase) Zenpep® DR (pancrelipase)	Aldurazyme® (laronidase) [MB] Carbaglu® (carglumic acid)*[PD BP] Cerdelga® (eliglustat) Cerezyme® (imiglucerase) [MB] Dojolvi® (triheptanoin) Elaprase® (idursulfase) [MB] Elelyso® (taliglucerase alfa) [MB] Fabrazyme® (agalsidase beta) Galafold® (migalastat) Kanuma® (sebelipase alfa) Kuvan® (sapropterin)* Lumizyme® (alglucosidase alfa) [MB] Mepsevii® (vestronidase alfa-vjbk) [MB] Naglazyme® (galsulfase) [MB] Nexviazyme® (avalglucosidase alfa-ngpt) Nulibry® (fosdenopterin) [MB] Palynziq® (pegvaliase-pqpz) Pheburane® (sodium phenylbutyrate granules) Pyrukynd® (mitapivat) Revcovi® (elapegademase-lvlr)

	Ryplazim® (plasminogen, human-tvmh) Strensiq® (asfotase alfa) Sucraid® (sacrosidase)* † Vijoice® (alpelisib) Vimizim® (elosulfase alfa) MB Vpriv® (velaglucerase alfa) MB Xenpozyme® (olipudase alfa-rpcp) MB Xuriden® (uridine triacetate) † Zavesca® (miglustat)* BP

* A-rated generic available. Both brand and A-rated generic require PA.
# This designates a brand-name drug with FDA "A"-rated generic equivalents. Prior authorization is required for the brand, unless a particular form of that drug (for example, tablet, capsule, or liquid) does not have an FDA "A"-rated generic equivalent.
BP Brand Preferred over generic equivalents. In general, requires a trial of the preferred drug or clinical rationale for prescribing the non-preferred drug generic equivalent.
PD preferred drug. In general, requires a trial of the preferred drug or clinical rationale for prescribing a non-preferred drug within a therapeutic class. **Please note, for Enzyme and Metabolic Disorder Therapies, a trial with Carbaglu is not required prior to approval of a non-preferred agent.**
MB This drug is available through the health care professional who administers the drug or in an outpatient or inpatient hospital setting. The plan does not pay for this drug to be dispensed through the retail pharmacy
†This agent does not participate in federal rebate. Please see the Non-FDA approved and Non-rebate products guideline for more information. Please note, drug-specific criteria may also apply as shown in the procedure table below.

Coverage Guidelines
Authorization may be reviewed on a case by case basis for members who are new to the plan currently receiving treatment with requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization will be granted when all the following criteria has been met, and documentation has been submitted:

Aldurazyme® (laronidase)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Mucopolysaccharidosis I (MPS I)
2. Results from genetic testing showing mutations in IDUA gene or an enzyme assay test showing reduced lysosomal alpha-L-iduronidase activity in peripheral blood leukocytes, plasma, or cultured fibroblasts
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Carbaglu® (carglumic acid)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of NAGS deficiency
2. Results from genetic test or an enzyme assay test (i.e., liver biopsy) supporting the diagnosis
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Appropriate dosing

Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hyperammonemia due to propionic aciduria (PA) or methylmalonic aciduria (MMA)
2. Results from genetic testing, medical records, or lab results supporting the diagnosis
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Elevated ammonia levels >60 µmol/L
5. Appropriate dosing

Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of *acute hyperammonemia in isovaleric aciduria (off-label)*
2. Medical records and/or laboratory testing results supporting the diagnosis of IVA
3. Abnormally elevated baseline ammonia levels (e.g., >60 µmol/L)
4. Appropriate dosing (see Availability and Dosage table below)

Cerdelga® (eliglustat)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Gaucher disease (Type I)
2. Member is ≥18 years of age
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Results from an enzyme assay test showing reduced activity of the enzyme glucocerebrosidase
5. Documentation showing that member is NOT currently receiving enzyme replacement therapy (ERT) (i.e., Cerezyme® [imiglucerase], Vpriv® [velaglucerase alfa] or Elelyso® [taliglucerase alfa])

Cerezyme® (imiglucerase)
Vpriv® (velaglucerase alfa*)*
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Gaucher disease (Type I)
2. Results from genetic test confirming mutation in GBA gene or an enzyme assay test showing reduced activity of the enzyme glucocerebrosidase
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Dojolvi® (triheptanoin)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of long chain fatty acid oxidation disorder (LC-FAOD)
2. Results from genetic testing or molecular analysis to confirm diagnosis (e.g., CPT I or II, LCHAD, TFP, VLCAD deficiency)
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Documentation of a trial with a diet consisting of low-fat, high-carbohydrates, and avoidance of fasting
5. Member's current caloric intake *(use to verify correct dosing)*

Elaprase® (idursulfase)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Hunter Syndrome (Mucopolysaccharidosis II)
2. Results from genetic testing confirming mutation in IDS gene or iduronate-2-sulfatase assay test showing reduced or absent activity in the serum, white blood cells, or fibroblasts

3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Elelyso® (taliglucerase alfa)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Gaucher disease (Type I)
2. Results from genetic test confirming mutation in GBA gene or an enzyme assay test showing reduced activity of the enzyme glucocerebrosidase
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member is ≥ 4 years of age
5. Member's current weight *(use to verify correct dosing)*

Fabrazyme® (agalsidase beta)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Fabry disease
2. One of the following confirming diagnosis:
    a. Results from an enzyme assay test showing reduced or absent α-GAL enzyme activity in plasma, leukocytes, tears, or biopsied tissue
    b. Genetic testing confirming mutation in GAL gene
    c. Biomarker demonstrating an increase in Gb3 (or GL-3) concentration
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Galafold® (migalastat)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Fabry disease
2. Member is ≥18 years of age
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Results from an enzyme assay test showing reduced or absent α-galactosidase A (α-GAL) enzyme activity in plasma, leukocytes, tears, or biopsied tissue
5. Member has GLA variants (mutations) which are amenable to treatment with migalastat (based on genetics consult notes)
6. Requested quantity is ≤15 units/30 days (0.5 units/day)

Kanuma® (sebelipase alfa)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of lysosomal acid lipase deficiency
2. **ONE** of the following:
    a. Lab assay documenting low lysosomal acid lipase activity
    b. Genetic testing confirming full or partial loss of LAL gene
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Kuvan® (sapropterin)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of phenylketonuria
2. Results from molecular analysis to confirm diagnosis
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Documentation that medication will be used in conjunction with a phenylalanine-restricted diet
5. Member's current weight *(use to verify correct dosing)*
6. If the request is for BRAND NAME Kuvan®, member must meet the above criteria and provide medical records documenting an inadequate response or adverse reaction to generic sapropterin (as per the Brand Name and Non-Preferred Generic Drugs guideline)

Lumizyme® (alglucosidase alfa)*
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of Pompe Disease
2. **ONE** of the following confirming diagnosis:
    a. Results from GAA assay test showing reduced or absent activity from cultured skin fibroblasts
    b. lymphocyte testing
    c. blood spot assay
    d. genetic testing confirming mutation in GAA gene
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

* Lumizyme® and Nexviazyme® should not be used concurrently

Mepsevii® (vestronidase alfa-vjbk)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
2. Results from genetic testing showing mutations in the beta glucuronidase gene
3. Prescriber is a specialist in genetic or metabolic diseases or provides documentation of a consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Naglazyme® (galsulfase)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of Mucopolysaccharidosis VI (MPS VI)
2. Results from an enzyme assay test showing reduced arylsulfatase B (ASB) enzyme activity in leukocytes or fibroblasts along with elevated urine glycosaminoglycan (GAG) levels
3. Prescriber is a specialist in genetic or metabolic diseases or provides documentation of a consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Nexviazyme® (avalglucosidase alfa-ngpt) *
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of late-onset Pompe Disease
2. **ONE** of the following confirming diagnosis:
    a. results from GAA assay test showing reduced or absent activity from cultured skin fibroblasts

b. lymphocyte testing
c. blood spot assay
d. genetic testing confirming mutation in GAA gene

3. Member is ≥ one year of age
4. Prescriber is a specialist in genetic or metabolic diseases or consult notes from a specialist are provided.
5. Member's current weight *(use to verify correct dosing)*
6. For members weighing < 30 kg, contraindication to Lumizyme®

* Lumizyme® and Nexviazyme® should not be used concurrently

Nulibry® (fosdenopterin)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of molybdenum cofactor deficiency (MoCD) Type A confirmed by genetic testing
2. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
3. Appropriate dosing
4. Member's current weight *(use to verify correct dosing)*

Palynziq® (pegvaliase-pqpz)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of phenylketonuria
2. Member is ≥ 18 years of age
3. Results from molecular analysis to confirm diagnosis
4. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
5. Documentation of blood phenylalanine concentrations >600 micromol/L
6. Documentation that medication will be used in conjunction with a phenylalanine-restricted diet
7. Physician attestation of inadequate response, adverse reaction, or contraindication to sapropterin

Pheburane® (sodium phenylbutyrate granules)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of urea cycle disorder (UCD)
2. Results from genetic test or an enzyme assay test (liver biopsy, fibroblast from skin biopsy, or red blood cells) supporting the diagnosis
3. Prescriber is a specialist in genetic or metabolic diseases or consult notes from a specialist are provided
4. Physician attestation of inadequate response or adverse reaction to **ONE** or contraindication to **BOTH** of the following*:*
    a. sodium phenylbutyrate powder
    b. sodium phenylbutyrate tablet
5. Appropriate dosing

* Requests noting inability to tolerate sodium phenylbutyrate powder or tablet formulations due to unpleasant taste will be evaluated on a case-by-case basis, taking into consideration whether a masking agent (e.g., chocolate syrup or peanut butter) or the taste-masked pellet formulation was tried.

Pyrukynd® (mitapivat)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hemolytic anemia with pyruvate kinase deficiency

2. Member is ≥ 18 years of age
3. Results from genetic testing confirming mutation in PKLR gene or lab testing showing reduced or absent activity of pyruvate kinase
4. Prescriber is a specialist in genetic diseases, hematology, or metabolic diseases or consultation notes from a specialist are provided
5. Hb ≤ 10 g/dL (dated within the last 60 days)
6. Requested quantity is ≤ 2 units/day

Revcovi® (elapegademase-lvlr)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of adenosine deaminase severe combined immunodeficiency (ADA-SCID)
2. Laboratory results documenting **ONE** of the following:
    a. Absent ADA enzymatic activity in lysed erythrocytes
    b. Elevated levels of adenosine and deoxyadenosine in the urine and plasma
    c. A marked increase in deoxyadenosine triphosphate (dATP) levels in erythrocyte lysates
    d. A significant decrease in ATP concentration in red blood cells
    e. Absent or extremely low levels of N adenosylhomocysteine hydrolase in red blood cells
    f. Severe T cell deficiency manifested by lymphopenia and poor T cell responses to mitogens and antigens
    g. Absent thymic shadow on chest radiograph
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Ryplazim® (plasminogen, human-tvmh)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of PLGD type 1
2. History of lesions (external and/or internal) and symptoms consistent with a diagnosis of PLGD type 1 (e.g., ligneous conjunctivitis, ligneous gingivitis or gingival overgrowth, vision abnormalities, respiratory distress and/or obstruction, abnormal wound healing)
3. Baseline plasminogen activity level ≤45%
4. ONE of the following:
    a. Results from genetic testing showing mutations in PLG gene
    b. Member has plasminogen antigen levels ≤9 mg/dL
5. Requested dose is ≤ 6.6 mg/kg every two to four days

Strensiq® (asfotase alfa)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of perinatal-onset, infantile-onset or juvenile-onset hypophosphatasia
2. Genetic testing confirming mutation in ALPL gene
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Sucraid® (sacrosidase)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of congenital sucrase-isomaltase deficiency (CSID)

2. Results from small bowel biopsy or breath hydrogen test showing reduced or absent enzyme activity or sucrase breath test
3. Prescriber is a specialist in genetic or metabolic diseases, a gastroenterologist, or consultation notes from a specialist or gastroenterologist are provided
4. Member's current weight *(use to verify correct dosing)*

Vijoice® (alpelisib)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of PROS with congenital or early childhood onset*
2. Member is ≥ 2 years of age
3. Overgrowth is sporadic and mosaic (i.e., patchy, irregular)
4. Results from genetic testing showing evidence of a mutation in the PIK3CA gene
5. Medical records documenting **ONE** of the following:
    a. Spectrum categorization defined as having at least **TWO** of the following:
        i. Adipose, muscle, nerve, or skeletal overgrowth
        ii. Capillary, venous, arteriovenous, or lymphatic vascular malformations
        iii. Epidermal nevus
    b. Isolated features defined as having **ONE** of the following:
        i. Large isolated lymphatic malformation
        ii. Isolated macrodactyly or overgrown splayed feet/hands, overgrown limbs
        iii. Truncal adipose overgrowth
        iv. Bilateral hemimegalencephaly/dysplastic megalencephaly/focal cortical dysplasia type 2
        v. Epidermal nevus
        vi. Seborrheic keratoses
        vii. Benign lichenoid keratoses
6. Appropriate dosing

** The following are subtypes of PROS and are acceptable as meeting diagnosis criteria: CLAPO syndrome, CLOVES syndrome, diffuse capillary malformation with overgrowth (DCMO), dysplastic megalencephaly (DMEG), fibroadipose hyperplasia (FAH), fibroadipose overgrowth (FAO), hemihyperplasia multiple lipomatosis (HHML), fibro-adipose vascular anomaly (FAVA), facial infiltrating lipomatosis (FIL), HMEG, Klippel-Trenaunay syndrome (KTS), LON, macrodactyly, megalencephaly-capillary malformation syndrome (MCAP), muscular hemihyperplasia (HH)*

Vimizim® (elosulfase alfa)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Mucopolysaccharidosis IVA (Morquio A syndrome)
2. Member is ≥ 5 years of age
3. Results from an enzyme assay test showing reduced N-acetylgalactosamine-6-sulfatase activity in blood and/or skin cells
4. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
5. Member's current weight *(use to verify correct dosing)*

Xenpozyme® (olipudase alfa-rpcp)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) type B, or ASMD type A/B

2. Prescriber is a specialist (e.g., medical geneticist or a specialist familiar with lysosomal storage disorders) or consultation notes from a specialist are provided
3. ONE of the following:
    a. For members ≥ 18 years of age, **BOTH** of the following:
        i. DLco ≤ 70% of predicted normal value
        ii. Spleen volume ≥ 6 MN
    b. For members < 18 years of age, spleen volume ≥ 5 MN
4. Member does **NOT** have acute or rapidly progressive neurologic abnormalities
5. BOTH of the following:
    a. Member does **NOT** require invasive ventilatory support
    b. Member does **NOT** require noninvasive ventilatory support while awake for > 12 hours a day
6. Member's current weight *(use to verify correct dosing)*
7. Appropriate dosing

Xuriden® (uridine triacetate)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hereditary orotic aciduria (HOA)
2. Genetic testing confirming mutation in UMPS gene
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Zavesca® (miglustat)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of Gaucher disease (Type I)
2. Member is ≥18 years of age
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Results from an enzyme assay test showing reduced activity of the enzyme glucocerebrosidase
5. Contraindication to enzyme replacement therapy (ERT) (e.g., hypersensitivity, allergy or poor venous access)

Continuation of Therapy
Dojolvi: Reauthorization by physician will infer a positive response to therapy and dosing is appropriate based on updated member's caloric intake.

Ryplazim and **Nulibry**: Reauthorization will require physician documentation of a positive response to therapy or clinical rationale for continued use if dosing is appropriate based on updated member's weight where applicable.

Xenpozyme: Prescriber provides documentation of **BOTH** of the following:
1. Improvement from baseline in DLco and spleen volume
2. Updated member weight

All other agents: Reauthorization by physician will infer a positive response to therapy and dosing is appropriate based on member's weight where applicable.

Limitations

1. Initial approvals will be granted for the following:
    a. Dojolvi, Nulibry, Palynziq, Vijoice, Xenpozyme: 6 months
    b. Ryplazim: 24 weeks
    c. All other agents: 1 year
2. Reauthorizations will be granted for the following:
    a. Xenpozyme – improvement in DLco and spleen volume: 6 months
    b. All other agents: 1 year
3. Members who are stable on Nulibry® (fosdenopterin) must meet both the initial and reauthorization criteria for approval.
4. The following quantity limits apply:

Galafold (migalastat)	15 units per 30 days
Pyrukynd (mitapivat)	60 units per 30 days

Appendix

Brand Preferred over Generic:

Requests for generic versions listed below require a trial of the preferred drug or clinical rationale for prescribing the non-preferred drug generic equivalent prior to approval:

- carglumic acid
- miglustat

References

1. Gieselmann V. Lysosomal storage diseases. Biochim Biophys Acta. 1995 Apr 24;1270(2-3):103-36. PMID: 7727535.
2. Bruni S, Loschi L, Incerti C, Gabrielli O, Coppa GV. Update on treatment of lysosomal storage diseases. Acta Myol. 2007 Jul;26(1):87-92. PMID: 17915580.
3. Wilcox WR. Lysosomal storage disorders: the need for better pediatric recognition and comprehensive care. J Pediatr. 2004 May;144(5 Suppl):S3-14. PMID: 15126978.
4. Lachmann R. Treatments for lysosomal storage disorders. Biochem Soc Trans. 2010 Dec;38(6):1465-8. PMID: 21118108.
5. Beck M. Therapy for lysosomal storage disorders. IUBMB Life. 2010; 62(1):33-40.
6. Aldurazyme® [package insert on the internet]. Cambridge (MA): Genzyme Corporation; 2019 July [cited 2021 Jun 29]. Available from: http://www.aldurazyme.com.
7. Han S. Mucopolysaccharidoses: clinical features and diagnosis. UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from http://www.utdol.com/utd/index.do.
8. Wraith JE, Clarke LA, Beck M, Kolodny EH, Pastores GM, Muenzer J, et al. Enzyme replacement therapy for mucopolysaccharidosis I: A randomized, double-blinded, placebo-controlled, multinational study of recombinant human alpha-L-iduronidase (laronidase). J Pediatr 2004 May; 144(5):581-8.
9. National Organization for Rare Diseases. Mucopolysaccharidosis Type I [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/mucopolysaccharidosis-type-i/.
10. Cerezyme® [package insert on the internet]. Cambridge (MA): Genzyme Corporation; 2018 Apr [cited 2022 Jan 26]. Available from: https://www.cerezyme.com/.
11. Hughes D. Gaucher disease: Pathogenesis, clinical manifestations, and diagnosis. UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from:
12. National Organization for Rare Diseases. Gaucher Disease [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/gaucher-disease/.

13. Dojolvi® [package insert]. Novato (CA): Ultragenyx Pharmaceutical Inc.; 2021 Nov.
14. Merritt II JL, Vockley J. Overview of fatty acid oxidation disorders. In: Hahn S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: https://www-uptodate-com.umassmed.idm.oclc.org/contents/overview-of-fatty-acid-oxidation-disorders.
15. Elelyso® [package insert on the internet]. New York (NY): Pfizer Labs; 2021 Jul [cited 2022 Jan 26]. Available from: http://www.elelyso.com.
16. Elaprase® [package insert on the internet]. Cambridge (MA): Shire Human Genetic Therapies, Inc.; 2021 Sep [cited 2022 Jan 26]. Available from: http://www.elaprase.com.
17. National Organization for Rare Diseases. Mucopolysaccharidosis Type II [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/mucopolysaccharidosis-type-ii-2/.
18. Fabrazyme® [package insert on the internet]. Cambridge (MA): Genzyme Corporation; 2021 May [cited 2022 Jan 26]. Available from: http://www.fabrazyme.com.
19. Eng CM, Guffon N, Wilcox WR, Germain DP, Lee P, Waldek S et al. Safety and efficacy of recombinant human alpha-galactosidase. A replacement therapy in Fabry's disease. N Engl J Med. 2001; 345(1):9-16.
20. IDORSIA. Fabry Disease [webpage on the internet]. Allschwil (Switzerland): IDORSIA; ; 2022 [cited 2022 Jan 26]. Available from: https://www.idorsia.com/about-idorsia/target-diseases/fabry-ebook.
21. Galafold® [package insert]. Cranbury, (NJ): Amicus Therapeutics; 2021 Feb.
22. Amicus Therapeutics Launches Galafold™ (Migalastat) for Treatment of Fabry Disease in Italy. Amicus Therapeutics: 2018 Aug 10 [cited 2017 Mar 8] Available from: http://ir.amicusrx.com/news-releases/news-release-details/amicus-therapeutics-launches-galafoldtm-migalastat-treatment-0
23. Hughes D.A, Nicholls K, Shankar S.P, et al., Oral pharmacological chaperone migalastat compared with enzyme replacement therapy in Fabry disease: 18- month results from the randomized phase III ATTRACT study, J. Med. Genet. 54 (2017) 288–296.
24. Kanuma® [package insert on the internet]. Cheshire (CT): Alexion; 2015 Dec [cited 2021 Jun 29]. Available from: http://www.kanuma.com.
25. Bernstein DL, Hülkova H, Bialer MG, Desnick RJ. Cholesteryl ester storage disease: Review of the findings in 135 reported patients with an underdiagnosed disease. J Hepatol [Internet]. European Association for the Study of the Liver; 2013;58(6):1230–43. Available from: http://dx.doi.org/10.1016/j.jhep.2013.02.014.
26. National Center for Advancing Translational Sciences. Lysosomal acid lipase deficiency [webpage on the internet]. Gaithersburg (MD): National Center for Advancing Translational Sciences; 2021 [cited 2021 Apr 27]. Available from: https://rarediseases.info.nih.gov/diseases/12097/lysosomal-acid-lipase-deficiency.
27. National Center for Biotechnology Information. Wolman Disease [webpage on the internet]. Bethesda (MD): National Center for Biotechnology; 2020 [cited 2021 Apr 27]. Available from: https://www.ncbi.nlm.nih.gov/gtr/conditions/C0043208/.
28. Kuvan® [package insert on the internet]. Novato (CA): BioMarin Pharmaceutical; 2021 Feb [cited 2022 Jan 26]. Available from: http://www.kuvan.com/downloads/KUVAN_Prescribing_Information.pdf.
29. National Organization for Rare Diseases. Phenylketonuria [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/phenylketonuria/.
30. Bodamer OA. Overview of phenylketonuria. In: Hanh S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: http://www.utdol.com/utd/index.do.
31. Lumizyme® [package insert]. Cambridge (MA): Genzyme Corporation; 2020 Feb.

32. Merritt JL. Lysosomal acid alpha-glucosidase deficiency (Pompe disease, glycogen storage disease II, acid maltase deficiency). UpToDate [database on the internet]. Waltham (MA): UpToDate2021 [cited 2022 Jan 26]. Available from http://www.utdol.com/utd/index.do.
33. Nexviazyme® [package insert]. Cambridge (MA): Genzyme Corporation; 2021 Aug.
34. Mepsevii® [package insert] Novato (CA): Ultragenyx Pharmaceuticals; 2022 Dec.
35. Naglazyme® [package insert on the internet]. Novato (CA): BioMarin Pharmaceutical Inc.; 2019 Dec [cited 2022 Jan 26]. Available from: http://www.naglazyme.com.
36. Palynziq® [package insert on the internet]. Novato (CA): BioMarin Pharmaceutical; 2020 Nov [cited 2022 Jan 26]. Available from: https://www.palynziq.com.
37. Revcovi® [package insert] Gaithersburg (MD): Leadiant Biosciences Inc; 2020 Dec [cited 2022 Jan 26]. Available from: https://revcovi.com/.
38. Strensiq® [package insert on the internet] Cheshire (CT): Alexion Pharmaceuticals; 2020 Jun [cited 2022 Jan 26]. Available from: http://www.strensiq.com.
39. National Organization for Rare Diseases. Hypophosphatasia [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2021 [cited 2022 Jan 26]. Available from: https://rarediseases.org/rare-diseases/hypophosphatasia/.
40. Sucraid® [package insert on the internet]. Vero Beach (FL): QOL Medial LCC; 2021 Oct [cited 2022 Jan 26]. Available from: http://www.sucraid.net.
41. Treem WR, McAdams L, Stanford L, Kastoff G, Justinich C, Hyams J. Sacrosidase therapy for congenital sucrase-isomaltase deficiency. J Pediatr Gastroenterol Nutr. 1999 Feb;28(2):137-42.
42. Robayo-Torres CC, Opekun AR, Quezada-Calvillo R, et al. 13C-breath tests for sucrose digestion in congenital sucrase isomaltase-deficient and sacrosidase-supplemented patients. J Pediatr Gastroenterol Nutr. 2009;48(4):412-418. PMID:19330928.
43. Metabolic Solutions. Sucrose Breath Test [webpage on the internet]. Nashua (NH): Metabolic Solutions; 2014 [cited 2021 Apr 15]. Available from: https://www.metsol.com/wp-content/uploads/2014/04/Sucrose-Breath-Test.pdf.
44. Vimizim® [package insert]. Novato (CA): BioMarin Pharmaceutical, Inc.; 2019 Dec [cited 2022 Jan 26]. Available from: http://www.vimizim.com.
45. Hanh S. Mucopolysaccharidoses: Treatment. UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from http://www.utdol.com/utd/index.do.
46. Balasubramaniam S, Duley JA, Christodoulou J. Inborn errors of pyrimidine metabolism: clinical update and therapy. J Inherit Metab Dis. 2014 Sep; 37(5):687-98.
47. Vpriv® [package insert on the internet]. Cambridge (MA): Shire Human Genetic Therapies, Inc.; 2021 Nov [cited 2022 Jan 26]. Available from: http://www.vpriv.com.
48. Shire announces FDA approval of Vpriv (velaglucerase alfa for injection for the treatment of type 1 Gaucher disease [press release on the internet]. Cambridge (MA): Shire plc: 2010 Feb 26 [cited 2018 Mar 26]. Available from: https://www.shire.com/newsroom/2010/february/shire-announces-fda.
49. Xuriden® (uridine triacetate) [package insert]. Gaithersburg (MD): Wellstat Therapeutics Corporation; 2019 Dec.
50. National Organization for Rare Diseases. Hereditary Orotic Aciduria [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Apr 20]. Available from: https://rarediseases.org/rare-diseases/hereditary-orotic-aciduria/.
51. Pancreatic Enzyme Replacement Products containing Lipase, Protease, and Amylase. American Society of Health-System Pharmacists [webpage on the Internet]. Atlanta (GA): American Society of Health-System Pharmacists; Nov 2012 [cited 2018 Mar 26]. Available from: http://www.ashp.org/menu/DrugShortages/ResolvedShortages/Bulletin.aspx?id=619.
52. FDA Approves First Treatment for Molybdenum cofactor Deficiency Type A. [press release on the Internet]. Food and Drug Administration (US); 2021 Feb 26 [cited 2021 Jun 30]. Available from:

https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-molybdenum-cofactor-deficiency-type.
53. Shellhaas R. Etiology and prognosis of neonatal seizures. In Trobe J (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: http://www.utdol.com/utd/index.do.
54. National Institutes of Health. Molybdenum cofactor deficiency. Last updated 2021 Feb [cited 2022 Jan 26]. Available from: https://medlineplus.gov/genetics/condition/molybdenum-cofactor-deficiency/#frequency.
55. Nulibry® [package insert]. Boston (MA): Origin Biosciences, Inc.; 2021 Feb.
56. Zavesca® [package insert]. South San Francisco(CA): Actelion Pharmaceuticals US, Inc.; 2021 Jan.
57. Cerdelga® [package insert]. Waterford (Ireland): Genzyme Ireland, Ltd; 2021 Jul.
58. Hughes D. Gaucher disease: Treatment. In: Hanh S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: http://www.utdol.com/utd/index.do
59. Lee B. Urea cycle disorders: Clinical features and diagnosis. In: Hahn S. (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 May 11]. Available from: http://www.utdol.com/utd/index.do.
60. Carbaglu® [package insert]. Lebanon (NJ): Recordati Rare Diseases Inc.; 2021 Aug.
61. Bodamer OA. Organic acidemias: An overview and specific defects. In: Hahn S. and Patterson MC (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 Mau 11]. Available from: http://www.utdol.com/utd/index.do.
62. Diaz GA, Krivitzky LS, Mokhtarani M, Rhead W, Bartley J, Feigenbaum A, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. Hepatology. 2013 Jun;57(6):2171-9.
63. FDA approves treatment for anemia in adults with rare inherited disorder [press release on the Internet]. FDA; 2022 Feb 17 [cited 2022 May 17]. Available from: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-treatment-anemia-adults-rare-inherited-disorder.
64. Agios Announces FDA Approval of PYRUKYND® (mitapivat) as First Disease-Modifying Therapy for Hemolytic Anemia in Adults with Pyruvate Kinase Deficiency [press release on the Internet]. Agios Pharmaceuticals, Inc.; 2022 Feb 17 [cited 2022 May 17]. Available from: https://investor.agios.com/news-releases/news-release-details/agios-announces-fda-approval-pyrukyndr-mitapivat-first-disease.
65. Pyrukynd® [package insert]. Cambridge (MA). Agios Pharmaceuticals, Inc.; Feb 2022.
66. Pyrukynd® Approved Product Dossier. Cambridge (MA). Agios Pharmaceuticals, Inc.; Mar 2022
67. Vijoice® [package insert] East Hanover (NJ): Novartis Pharmaceuticals; 2022 April.
68. Alpelisib: drug information. In: Post T (Ed).UpToDate [database on the Internet]. Waltham (MA): UpToDate; 2022 [citied 2022 June 1]. Available from: http://www.utdol.com/utd/index.do.
69. National Organization for Rare Disorders: PIK3CA-Related Overgrowth Spectrum. Danbury (CT): NORD; 2022 [citied 2022 May 25]. Available from: https://rarediseases.org/rare-diseases/pik3ca-related-overgrowth-spectrum/.
70. Balwania M, Burrowb TA, Charrowc J, Goker-Alpand O, Kaplane P, Kishnani PS, et al. Recommendations for the use of eliglustat in the treatment of adults with Gaucher disease type 1 in the United States. Molecular Genetics and Metabolism; 117(2):95-103.
71. Schiffmann R, Fitzgibbon EJ, Harris C, DeVile C, Davies EH, Abel L, et al. Randomized, controlled trial of miglustat in Gaucher's disease type 3. Ann Neurol. 2008; 64(5):514-522.
72. Lee B. Urea cycle disorders: Management. In: Hahn S. (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; ; 2022 [cited 2022 Mar 22]. Available from: http://www.utdol.com/utd/index.do.

73. Caruthers RL, Johnson CE. Stability of extemporaneously prepared sodium phenylbutyrate oral suspensions. Am J Health Syst Pharm. 2007 Jul 15;64(14):1513-5.
74. Valayannopoulos V, Baruteau J, Delgado MB, Cano A, Couce ML, Del Toro M, et al. Carglumic acid enhances rapid ammonia detoxification in classical organic acidurias with a favourable risk-benefit profile: a retrospective observational study. Orphanet J Rare Dis. 2016 Mar 31;11:32.
75. XenpozymeTM [package insert]. Cambridge (MA): Genzyme Corporation.; 2022 Aug.
76. FDA Approves First Treatment for Acid Sphingomyelinase Deficiency, a Rare Genetic Disease [press release on the Internet]. Rockville (MD): Food and Drug Administration (US); 2022 Aug 31 [cited 2022 Dec 9]. Available from: http://www.fda.gov/bbs/topics/NEWS/2007/NEW01587.html.
77. Genzyme Corporation. XenpozymeTM (Olipudase alfa-rpcp) [webpage on the internet]. Cambridge (MA): Genzyme Corporation 2022 [cited 2022 November 20]. Available from: https://www.xenpozyme.com/
78. Wasserstein MP, Schuchman EH, Adam MP, Everman DP, Mirzaa GM, Pagon RA, et al. Acid Sphingomyelinase Deficiency. GeneReviews 2006 December 7. PMID: 20301544
79. McGovern MM, Avetisyan R, Sanson BJ, Lidove O. Disease manifestations and burden of illness in patients with acid sphingomyelinase deficiency (ASMD). Orphanet J Rare Dis. 2017 Feb 23;12(1):41.
80. National Organization for Rare Disorders (NORD). Acid Sphingomyelinase Deficiency [webpage on the internet]. Fort Atkinson (WI): NORD: 2021 [cited 2022 November 20]. Available from: https://rarediseases.org/rare-diseases/acid-sphingomyelinase-deficiency/
81. Patterson M. Overview of Niemann-Pick Disease. In: Basow DS (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 November 20]. Available from: http://www.utdol.com/utd/index.do.
82. Wasserstein M, Lachmann R, Hollak C, Arash-Kaps L, Barbato A, Gallagher RC, et al. A randomized, placebo-controlled clinical trial evaluating olipudase alfa enzyme replacement therapy for chronic acid sphingomyelinase deficiency (ASMD) in adults: One-year results. Genet Med. 2022 Jul;24(7):1425-1436.
83. Diaz GA, Jones SA, Scarpa M, Mengel KE, Giugliani R, Guffon Net al. One-year results of a clinical trial of olipudase alfa enzyme replacement therapy in pediatric patients with acid sphingomyelinase deficiency. Genet Med. 2021 Aug;23(8):1543-1550.
84. XenpozymeTM (olipudase alfa) approved by European Commission as first and only treatment for ASMD [press release on the internet]. Paris (France): Sanofi; 2022 June 28. [cited 2022 November 28] Available from: https://www.sanofi.com/en/media-room/press-releases/2022/2022-06-28-05-30-00-2469974
85. Genzyme Corporation. XenpozymeTM (Olipudase alfa-rpcp) Billing and Coding Guide [webpage on the internet]. Cambridge (MA): Genzyme Corporation 2022 [cited 2022 November 20]. Available from: https://www.xenpozyme.com/

Review History

02/08/2023 - Reviewed and created for Feb P&T; matched MH UPPL. Created criteria to be in compliance with Masshealth unified formulary requirements (Effective 4/1/23).
05/10/23 – Reviewed and updated for P&T. Added new drug, Ryplazim® (plasminogen, human-tvmh), to policy. Added initial and reauthorization criteria for Xenpozyme for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. A noted was added for Fabrazyme to clarify that Gb3 may be referred to as GL-3. References updated. Effective 6/5/23